REMARKS/ARGUMENTS

Claims 1-24 are pending in the present application. The subject claims are all canceled in this Amendment, without prejudice or disclaimer, in favor of new claims 25-32, which are believed to more clearly recite applicants' invention. The new claims are all completely supported by the application as originally filed and thus they do not raise any issue of new matter. Entry of these new claims into the file of this application is, therefore, respectfully requested.

Further to the above, the specification has been amended at a number of locations to correct certain translation errors which applicant has become aware of in the English-language translation of the corresponding International application, which was originally filed in the Spanish language (i.e., PCT/ES02/00194 published as WO 03/089425). No new matter is added by these corrections as they are all supported by the original Spanish text of the International application. Entry of these specification amendments is, thus, also respectfully requested.

Claim Rejections Under 35 USC 112

Claims 1-24 are rejected under 35 USC 112, second paragraph, due to alleged indefiniteness.

In the first ground for rejection, the Examiner alleges that the term "polymorph 1" in claims 1-18 is ambiguous and indefinite. In response, applicants submit that none of the new claims 25-32 provided herewith contain the term "polymorph 1". Instead, applicants have adopted the language suggested by the Examiner and the claims thus recite the "crystalline form 1 of bilastine". This language is believed to overcome the above-mentioned objection, which should therefore be withdrawn.

In the next ground for rejection, the Examiner alleges that the phrase, "at least one of isopropylic acid and n-butanol" in claims 19-24 is confusing. In response, as presently presented new claims 31-32 contain the phrase, "is isopropylic alcohol or n-butanol". This language is believed to overcome the Examiner's objection, which should thus be withdrawn.

In the next ground for rejection, the Examiner objects to the phrase, "preparing a medicinal product for treating allergic reactions and pathological processes mediated by histamine" as being confusing. In response to this ground of rejection, applicants have redrafted

old claim 12, i.e., now new claim 30, in a manner which is believed to overcome the Examiner's objection. Applicants, therefore, respectfully request the Examiner to reconsider and withdraw the objection to the subject claim.

Further to the above, claims 1-3 and 15-18 are rejected under 35 USC 112, first paragraph, as allegedly failing to comply with the enablement requirement of the statute. In response, applicants have provided a set of new claims for the Examiner's review and consideration that are written in a manner that is believed to overcome the ground for rejection. Each new claim represents, in essence, a combination of several of the originally filed claims wherein each such new claim is believed to be entirely enabled by the teaching contained in the as-filed specification. In particular, the new claims are based upon the following combination of original claims: new claim 25 = original claims 1 + 2 +3; new claim 26 = original claims 4 + 15 + 16; new claim 27 = original claims 5 + 17 + 18; new claim 28 = original claims 6 + 7 + 8; new claim 29 = original claims 9 + 10 + 11; new claim 30 = original claims 12 + 13 + 14; new claim 31 = original claims 19 + 21 + 22; and new claim 32 = original claims 20 + 23 and 24. The Examiner is, therefore, respectfully requested to reconsider and withdraw the rejection under 25 USC 112, first paragraph.

In addition, in paragraph 4 of the Office Action claims 15-18 are rejected under 35 USC 112, first paragraph, as allegedly failing to meet the enablement requirement of the statute. In response, applicants respectfully submit they believe that due to the cancellation of the rejected claims in this response (without prejudice or disclaimer), the rejection of the subject claims has been rendered moot and should therefore be withdrawn.

Still further, claims 4-5 and 15-18 stand rejected (Office Action, paragraph 5) under 35 USC 112, first paragraph, as allegedly failing to meet the enablement requirement of the statute. The Examiner objects to the subject claims as allegedly failing to include 'critical' elements such as temperature, time, concentration, kind and ratio of the mixture of solvents, etc. In response, applicants submit that they have rewritten original claims 4 and 5 (now new claims 26-27) such that the subject claims recite a process which comprises heating from ambient temperature (i.e., 25-30°C) up to the reflux temperature of the corresponding solvent (see, e.g., Examples 1-5). Further to the above, applicants respectfully submit that the remaining process parameters, e.g., concentration, reaction time, ratio of solvents, etc., would be readily ascertained by one of ordinary skill in this art from the information provided in, for example, Examples 1-5 in the

present specification, without the need for any undue experimentation. Applicants respectfully submit, therefore, that it is believed one having ordinary skill in this art could readily practice the process recited in the present replacement claims without the need for any undue experimentation and, as such, the replacement claims submitted herewith are believed to meet all of the requirements for enablement under 35 USC 112. The Examiner is, therefore, respectfully requested to reconsider and withdraw the rejection of claims 4-15 and 15-18 under 35 USC 112, first paragraph.

Additionally, in paragraph 6 at pps. 5-7 of the Office Action, claims 9-14 are rejected under 35 USC 112, first paragraph as allegedly failing to comply with the enablement requirement of the statute.

In response, the rejected claims have been rewritten as corresponding new claims 29 – 30 directed to a pharmaceutical preparation and to a method of making such a pharmaceutical preparation. The Examiner, in the Office Action, indicates that in the preparation process there are a number of factors that could lead to a transformation of bilastine into different crystalline forms and that the description of the preparation of the pharmaceutical composition as contained in applicants' specification is not explicitly shown to have the IR or X-ray diffraction spectra described on p. 2 of the application or in Figs. 1-3. It is respectfully submitted, however, in response that it would be well known to one having an ordinary degree of skill in this art at the time the present invention was made both that it is important to maintain control of the crystalline form of the bilastine and, in addition, how to maintain such control over the crystalline form. That is to say that both of these issues are well within the province of one having an ordinary level of skill in the subject art and, thus, both steps are capable of being accomplished by such an individual without the need for any undue experimentation.

For the reasons presented above, therefore, the Examiner is respectfully requested to reconsider and withdraw the rejection of claims 9-14 under 35 USC 112, first paragraph.

Claim Rejections Under 35 USC 102/103

Original claims 6-10 are rejected under 35 USC 102(b) as allegedly anticipated by Orjales et al. US Patent No. 5,877,187, or *alternatively*, original claims 1-3 are rejected for 'obviousness' under 35 USC 103 over Orjales et al. USP 5,877,187 in view of Rowland and Tozer supplemented with Corcostegui et al. The reasons in support of these alternate grounds of

rejection are provided on pps. 7-8 of the Office Action. These rejections are respectfully traversed.

The Examiner indicates, in support of the 'anticipation' rejection, that the histaminic/antiallergenic effect and the pharmaceutical preparation defined in original claims 6-10 are taught by the Orjales et al. reference. With respect to such disclosure, the Examiner indicates that when the crystalline form 1 (of bilastine) is formulated as a liquid pharmaceutical product, the crystalline material becomes solvated, following which its effect is the same as that disclosed in the Orjales et al. reference.

In response to this rejection, applicants respectfully note that the Orjales et al. reference discloses that bilastine is obtained as a 'crude' product having a melting point range of from 199-201 °C. The melting point of pure crystalline form 2 is 205.2°C whereas the melting point of pure crystalline form 3 is 197 °C, as taught by applicants (see, e.g., p. 4, lines 10-11). From this it is apparent, therefore, that the crude product disclosed in the reference is comprised of a mixture of crystalline forms 2 and 3 of bilastine. It does not consist of pure crystalline form 2, or pure crystalline form 3 or a mixture of the pure crystalline forms. In summary, therefore, the histaminic/antiallergenic properties produced as described in the Orjales et al. reference are produced by a mixture of crystalline forms 2 and 3, and not by a composition containing the crystalline form 1 of bilastine as recited in new claims 28 and 29, which have taken the place of original claims 6-10.

Still further, taking into account the Examiner's point that a solid will loose its crystalline structure when it is solvated by a solvent, applicants respectfully submit that new claims 28-29 as now formulated recite a pharmaceutical preparation and a method for making the same wherein the active ingredient (i.e., the crystalline form 1 of bilastine) is not solvated but, rather, is in a solid form. Support for the claims to these embodiments is found at pps. 8-10 of applicants' specification, which separately describes solid and liquid preparations. In light of the Examiner's remarks, therefore, applicants' have elected to limit their claims to the pharmaceutical preparation and the method of making the same to the solid form of the preparation while excluding 'solutions', i.e., wherein the crystalline form becomes solvated.

For the reasons above, the Examiner is respectfully requested to reconsider and withdraw the rejection of original claims 6-10 under 35 USC 102.

Still further, concerning the Examiner's 'obviousness' rejection of original claims 1-3 under 35 USC 103, the Examiner alleges that a histaminic/antiallergenic effect of 'crystalline form 1 of bilastine' would be expected (i.e., 'obvious') upon the absorption and distribution stages of the active ingredient in the body of a subject (see Rowland and Tozer), as well as at the cellular level. The Examiner further concludes that one of ordinary skill in this art would be prompted to modify the teachings contained in the Orjales et al. reference by searching for a 'purer' form of bilastine, particularly so when such modifications are viewed as a 'routine practice', as evidenced by the trial disclosed in Corcostegui et al.

To begin with, applicants respectfully submit that Corcostegui et al. is not prior art to the present invention as the publication date thereof is 2005, whereas the present U.S. application is a National Stage filing of an earlier International Application (PCT/ES02/00194) bearing a filing date of April 19, 2002, i.e., three years before the publication of Corcostegui et al. Removal of Corcostegui et al. as a reference against the present application is, therefore, respectfully solicited.

With regard to the remaining references, moreover, applicants respectfully submit that the crystalline form 1 of bilastine as now recited in claim 25 (which replaces original claims 1-3) is not a 'purified' form of the material. That is, the process for obtaining the crystalline material recited by the claim does not increase the purity of the resultant bilastine. As noted above, the disclosure of the primary reference, i.e., Orjales, et al. leads to the production a crude bilastine product, which comprises a mixture of crystalline forms 2 and 3, in contrast to the material which is recited in claim 25, which is a crystalline form 1 of bilastine. This material is the only form of bilastine known that is thermally stable and, thus, it is the only form appropriate for use in forming a pharmaceutical product (as is also recited in several of the other claims pending in this application). The claimed material, i.e., crystalline form 1 of bilastine, can not, moreover, be obtained with the use of the method disclosed in Orjales et al.

For the reasons presented above, therefore, the Examiner is respectfully requested to withdraw the rejection of claims 1-3 under 35 USC 103.

In addition to the above, original claims 4-5 and 16-24 are rejected as allegedly 'obvious' under 35 USC 103 over Orjales et al. USP 5,877,187 in view of Cheronis for the reasons given at pp. 8-9 of the Office Action. This rejection is respectfully traversed.

According to the Office Action, the subject claims do not display an inventive step because the difference between the method as defined in the claims and the method as disclosed in the Orjales et al. patent involves 'only' the selection of solvents used in a final stage of purification involving a crystallization step, whereupon the Examiner argues that purification by crystallization is a routine practice per the disclosure contained in the Cheronis reference.

In response applicants again submit to the Examiner that, as noted above the preparation of crystalline form 1 of bilastine does not involve a purification due to the fact that the process of obtaining this material does not increase the purity of the bilastine. What is produced, i.e., the crystalline form 1 of bilastine is a material which is not obtained through the process described in the primary reference, i.e., the US Orjales et al. patent. Moreover, further to the above, applicants contend that one having ordinary skill in this area would find no motivation in the prior art cited to reject the original claims of this case to "purify" the product produced according to Orjales et al.

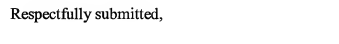
The Examiner is, thus, respectfully requested to reconsider and withdraw the rejection of original claims 4-5 and 16-24 under 25 USC 103.

Summary

The new claims presented in this response are believed to distinguish applicants' invention over the prior art cited to reject original claims 1-24, in light of the remarks presented above. The Examiner is, thus, respectfully requested to reconsider and withdraw the presently pending grounds for rejection and to issue a Notice of Allowance regarding this application.

THIS CORRESPONDENCE IS BEING SUBMITTED ELECTRONICALLY THROUGH THE PATENT AND TRADEMARK OFFICE EFS FILING SYSTEM ON April 24, 2008.

Respectfully submitted,



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